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Enclosure:

- POSTER: Ward CL, Oberdhan D, Jin N, et al. Presented at Psych Congress, September 17-21, 2025; San Diego, CA, USA.

Efficacy of Centanafadine on Conners 3 Content Scales in Adolescents With Attention-Deficit/ Hyperactivity Disorder

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INTRODUCTION

- Attention-deficit/hyperactivity disorder (ADHD) is one of the most common pediatric neurodevelopmental disorders, characterized by symptoms of inattention, hyperactivity, and impulsivity—all of which can affect overall quality of life for patients and their families[1,2]
- Individuals with ADHD can also have impairments in executive functioning or high-level cognitive processes that include inhibition, switching between tasks, working memory, planning, monitoring, and verbal and design fluency[3]
- The Conners 3–Parent Short (PS; children and adolescents) and Conners 3–Self-Report Short (SRS; adolescents only) Content Scales measure symptoms of inattention, hyperactivity, and impulsivity. The Conners 3–PS Content Scales can also measure some aspects of executive functioning[4]
- A phase 3 trial of adolescents aged 13–17 years evaluated the efficacy and safety of once-daily, extended-release centanafadine (CTN), a norepinephrine, dopamine, serotonin reuptake inhibitor, for the treatment of ADHD

OBJECTIVE

- To evaluate the treatment impact of CTN on inattention, hyperactivity/impulsivity, and executive functioning via caregiver- and/or self-report in adolescents with ADHD

METHODS

- **Study:** A phase 3, multicenter, randomized, double-blind, placebo-controlled trial conducted in the United States and Canada (NCT05257265)
- **Eligible participants:** Adolescents (13–17 years) with a primary diagnosis of ADHD (of any presentation) according to *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) criteria, as confirmed by the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID)
- **Treatment:** Participants were randomized (1:1:1) to receive once-daily extended-release CTN 328.8 mg, CTN 164.4 mg, or placebo for 6 weeks without an initial titration
- **Efficacy outcomes:** Change from baseline in the Conners 3–PS (caregiver perspective) and Conners 3–SRS (adolescent perspective) for the Inattention, Hyperactivity/Impulsivity, and Executive Functioning (Conners 3–PS only) Content Scale T-scores at Week 6
- **Analysis:** Outcomes were analyzed using a mixed-effect model for repeated measures
  - Values presented are least squares mean change from baseline (standard error)
  - CTN 164.4 mg did not meet the primary endpoint; thus, CTN 164.4 mg has been excluded from this presentation of secondary and/or exploratory endpoints and presented *P*-values were not controlled for multiplicity
- **Other outcomes:** Safety and tolerability

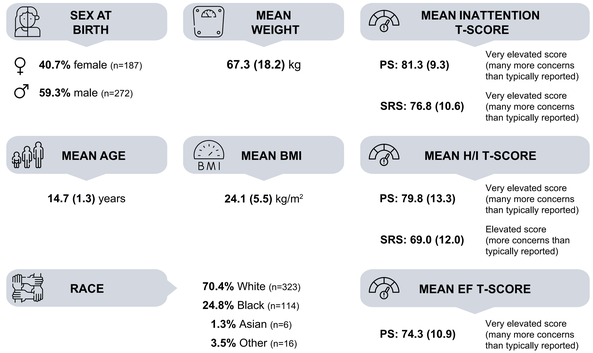
RESULTS

- Overall, 80.8% (371/459) of adolescents (mean age 14.7 years, 59.3% male) completed the study (**Figure 1**)
- Improvements from baseline in the Inattention Content Scale T-scores were reported by caregivers for CTN 328.8 mg versus placebo (Conners 3–PS: −14.4 [1.0] *vs* −8.1 [1.0], *P*<0.0001) and were self-reported by adolescents (Conners 3–SRS: −15.3 [1.1] *vs* −10.0 [1.0], *P*=0.0001) (**Figure 2**)
- Improvements from baseline in the Hyperactivity/ Impulsivity Content Scale T-scores were reported by caregivers for CTN 328.8 mg versus placebo (Conners 3–PS: −14.0 [1.1] *vs* −8.5 [1.1], *P*=0.0002) and were self-reported by adolescents (Conners 3–SRS: −11.6 [0.9] *vs* −8.9 [0.9], *P*=0.0282) (**Figure 3**)
- Similarly, improvements in Executive Functioning Content Scale T-Scores were observed for CTN 328.8 mg versus placebo on the Conners 3–PS (−13.0 [1.0] *vs* −8.1 [1.0], *P*=0.0003) (**Figure 4**). The Conners 3–SRS does not include the Executive Functioning Content Scale

Safety

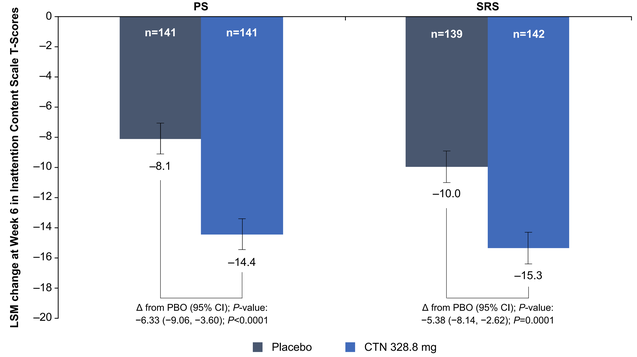
- Most treatment-emergent adverse events were mild to moderate, with the most common (≥5% in the CTN 328.8-mg group and greater than placebo) being decreased appetite (15.2%), nausea (9.9%), headache (6.0%), and rash (6.0%)

Figure 1. Baseline demographics and clinical characteristics of all randomized adolescents (N=459)



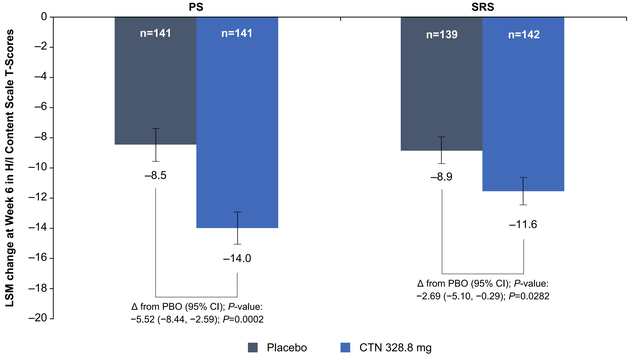
Means are presented with standard deviations. For race, the "Other" category includes participants who self-identified as American Indian / Alaskan Native, Native Hawaiian / Other Pacific Islander, or "other." BMI, body mass index; EF, Executive Functioning; H/I, Hyperactivity/Impulsivity; PS, Conners 3–Parent Short; SRS, Conners 3–Self-Report Short.

Figure 2. LSM change at Week 6 in Conners 3–PS and –SRS Inattention Content Scale T-scores



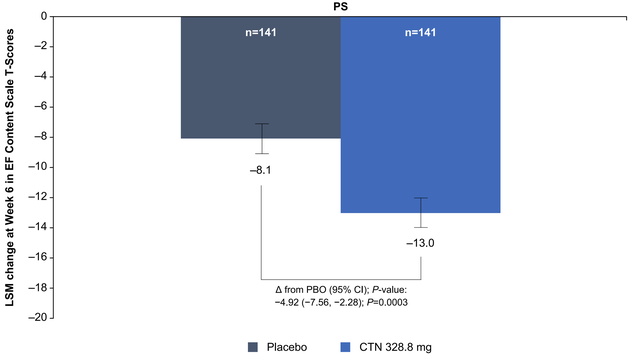
LSM change is derived from a mixed-effect model for repeated measures. Error bars are standard error of the means. CI, confidence interval; CTN, centanafadine; LSM, least squares mean; PBO, placebo; PS, Conners 3–Parent Short; SRS, Conners 3–Self-Report Short.

Figure 3. LSM change at Week 6 in Conners 3–PS and –SRS Hyperactivity/ Impulsivity Content Scale T-scores



LSM change is derived from a mixed-effect model for repeated measures. Error bars are standard error of the means. CI, confidence interval; CTN, centanafadine; H/I, Hyperactivity/Impulsivity; LSM, least squares mean; PBO, placebo; PS, Conners 3–Parent Short; SRS, Conners 3–Self-Report Short.

Figure 4. LSM change at Week 6 in Conners 3–PS Executive Functioning Content Scale T-scores



LSM change is derived from a mixed-effect model for repeated measures. Error bars are standard error of the means. CI, confidence interval; CTN, centanafadine; EF, Executive Functioning; LSM, least squares mean; PBO, placebo; PS, Conners 3–Parent Short.

CONCLUSIONS

- CTN 328.8 mg showed improvements in inattention, hyperactivity/impulsivity, and executive functioning symptoms in adolescent participants when compared to placebo, with both greater caregiver and adolescent perceptions of symptom improvement
- Once-daily extended-release CTN 328.8 mg was efficacious with a favorable safety profile in the treatment of ADHD in adolescents

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At Otsuka, we hold a deep respect for the value of every mind. We will not rest until mental illnesses and brain diseases are approached with the same priority and urgency as our physical health and recognized as chronic diseases that warrant early, equitable, and accessible intervention for patients and caregivers everywhere.

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